34. (once amended) The nutritional supplement according to claim 1, comprising a sterol ester of eicosapentaenoic acid 20:5ω3 (EPA) and a sterol ester of docosahexaenoic acid 22:6ω3 (DHA).

Please cancel claims 36 and 38.

REMARKS

Solely for the purposes of expediting prosecution, the claims have been amended to specify that the omega-3 fatty acid is selected from the group consisting of eicosapentaenoic acid 20:5ω3 (EPA), docosahexaenoic acid 22:6ω3 (DHA) and stearidonic acid 18:4ω3 (SA). These are the omega-3 fatty acids found in high concentration in fish oil. Support for the amendment is found in the specification at, e.g., page 6, lines 15-18.

A marked up version of the amended claims entitled "Version With Markings To Show Changes Made" is attached.

Concerning 35 USC § 112, First Paragraph

The Office Action provides that claims 1, 5-11, 34, 36, 38 and 39 stand rejected under 35 USC 112, first paragraph for the reasons set forth in the previous action (i.e. paper No. 16 mailed July 3, 2001).

In paper No. 16, the Examiner contended that:

> There are no examples in the specification showing any data for lowering cholesterol or triglycerides as has been instantly claimed. One example for the synthesis of the ester was found in the specification. Applicant's argument regarding the synthesis has been noted by the Examiner. The Examiner respectfully disagrees with the arguments because there is no data for what has been claimed. No example for how the invention will work is disclosed. Applicant must show support in terms of data *in vitro* or *in vivo* to support the claimed invention.
>
> One skilled in the art would have to do undue experimentation to practice the instant invention. There is no support for what has been claimed. Instantly claimed invention is drawn to nutrition supplement comprising a sterol ester of an omega fatty acid for lowering cholesterol and triglyceride levels in the blood stream of a subject. No examples or data is provided.

Applicant respectfully traverses this rejection and maintains that the claims as presently amended are fully enabled by the specification as filed.

There are two aspects to the Examiner's rejection under 35 USC 112, first paragraph:

(1) there are no examples in the specification showing any data for lowering cholesterol or triglycerides; and

(2) there is only one example for the synthesis of the ester contained in the specification.

Applicant will address these matters individually.

Concerning the alleged lack of data for lowering cholesterol or triglyceride levels, Applicant submits that the claimed invention is enabled if any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F. 2d at 737, 8 USPQ 2d at 1404 (Fed. Cir. 1988). Hence, the question is whether the specification is sufficient to enable a skilled person to make and use the claimed invention without undue experimentation. The instant specification contains sufficient information to allow the skilled person to use the nutritional supplements for lowering cholesterol and triglyceride levels. As noted in Applicant's previous response (paper No. 18), the specification provides, at page 3, lines 6-9 that the nutritional supplement comprising a sterol and an omega-3 fatty acid will have the effect of lowering cholesterol and triglyceride levels. Furthermore, the specification describes how the nutritional supplement may be included in foodstuffs so that one skilled in the art understands how the nutritional supplement may be used in practice (specification page 11, lines 9-19). Additionally, the specification provides guidance as to the amount of nutritional supplement that may be used (page 7, line 6 to page 8, line 15). Hence, the specification contains specific details of how to use the claimed nutritional supplements for lowering cholesterol and triglyceride levels.

Moreover, it has been held that, if a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of

administration are known and contemplated, 35 USC 112 is satisfied. *In re Johnson*, 282 F. 2d 370, 373, 127 USPQ 216, 219 (CCPA 1960).

In any event, it does not appear that the Examiner's concerns relate to any lack of instructions for how to use or administer the nutritional supplements of the invention, but rather that no working examples are provided to show that the claimed nutritional supplements are useful for reducing cholesterol and triglyceride levels. Applicant emphasizes that compliance with the enablement requirement of 35 USC 112, first paragraph, does not turn on whether an example is disclosed (MPEP 2164.02). A specification may not need contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F. 2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Again, Applicant submits that sufficient details are provided in the specification to make and use the claimed nutritional supplements, such that the enablement requirement is met.

As to the Examiner's contention that the claimed supplements have not been demonstrated to reduce cholesterol or triglyceride levels, Applicant again respectfully draws the Examiner's attention to the declaration of Dr. Stephen Ewart, filed with Applicant's amendment dated April 12, 2001. Dr. Ewart's declaration describes and includes data from experiments demonstrating that Applicant's claimed nutritional supplements are effective to lower both cholesterol and triglyceride levels in the blood of an animal. Applicant notes that a declaration or affidavit is, itself, evidence that must be considered (MPEP 2164.05).

In order to make a rejection for lack of enablement under 35 USC 112, first paragraph, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993). "It is incumbent upon the Patent Office, whenever a rejection [for lack of enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F. 2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

In the instant case, the Examiner has provided no rationale for lack of enablement other than that the specification does not contain working examples showing that the claimed nutritional supplements actually cause reduction of cholesterol or triglyceride levels. Apart from the Examiner's contention that there is only one example of a sterol omega-3 fatty acid provided in the specification, the Examiner has made no assertion or provided any reason basis or evidence that Applicant's specification fails to teach how to make and use the claimed nutritional supplement. As discussed above, the specification contains sufficient details of how to prepare the nutritional supplements and administer them.

The absence of test results in the specification showing that the claimed supplements are effective is not relevant to enablement — i.e. whether a person of ordinary skill in the art could make and use the invention based on the information contained in the specification as filed. That the nutritional supplements of the invention are useful are evidenced by the uncontroverted declaration of Dr. Stephen Ewart. It is irrelevant that this evidence is provide separately from the patent application. The patent application provides full details of how to make an use the claimed nutritional supplements, thereby meeting the enablement requirement. The declaration of Dr. Ewart obviates any question that the supplements have the claimed utility.

Turning to the second aspect of this rejection, the Examiner also contends that the claims lack enablement on the grounds that only a single example of sterol ester of an omega-3 fatty acid is provided in the specification. This is the only basis the Examiner puts forth for this rejection. No specific technical reasons are provided to support the Examiner's rejection. The Examiner has provided no explanation of why other sterols could not be used to synthesis the claimed invention. It has not been asserted by the Patent Office that the chemical properties of known sterols vary to such an extent that it would not be expected by one of ordinary skill in the art that any such sterol would react as expected by Applicant. As a result, there is no basis to conclude that one skilled in the art would not be able to prepare sterol esters of an omega fatty acid as described in the specification. Applicant respectfully submits that the Patent Office has not met its initial burden of establishing a reasonable basis to question the enablement of the present invention. As stated in *In re Marzocchi, supra*:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 USC 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. (emphasis added).

For the foregoing reasons, Applicant respectfully requests reconsideration and withdrawal of the rejections of the claims under 35 USC 112, first paragraph.

Concerning 35 USC 103

Claims 1, 5-11, 34, 36, 38 and 39 further stand rejected under 35 USC 103 as being unpatentable over Burdick *et al.* (EP 1,004,594) and Novak Egon (WO 00/04887) for the reasons set forth in the Office Action dated July 3, 2001.

Applicant respectfully traverses this rejection. The instant application was filed on August 30, 1999. The Burdick *et al.* reference was published on May 31, 2000, and the Novak Egon reference was published on February 3, 2000, both of which dates are after the instant filing date. Thus, the cited references are not prior art. Reconsideration and withdrawal of this rejection are therefore respectfully requested.

The Examiner reapplies the previous rejections of the claims under 35 USC 103(a) as being unpatentable over Miettinen *et al.* (EPA 594,612, WO 92/19640), Alexander Leaf *et al.* (The New England Journal of Medicine, vol. 318, No. 9, pages 549-557), and Mitchell (US Pat. No. 4,588,717).

Applicant again respectfully traverses this rejection and submits that the claims, as presently amended, patentably distinguish from the Miettenen *et al.*, Leaf *et al.* and Mitchell.

Miettenen *et al.* teach that plant sterols lower cholesterol by displacing dietary cholesterol in bile acid micelli (Miettenen *et al.* (EP 0 594 612 B1) page 2, lines 56-57). Miettenen *et al.* further teach that plant sterols in crystalline form do not to a significant degree dissolve in micelli phase, and are therefore not capable of efficiently inhibiting cholesterol absorption. Oils and fats are only to a limited degree capable of dissolving free sterols.

Only in a dissolved form do sterols inhibit the absorption of cholesterol (Miettenen *et al.*, page 3, lines 7-13).

Miettenen *et al.* teach that others have tried to overcome this insolubility problem by esterifying the sterol to a fatty acid moiety, to increase the solubility of the sterol, but that these esters were not of food-grade quality. Miettenen *et al.*'s contribution is to prepare the fatty acid ester of the sterol by way of a food-grade, solvent-free process (Miettenen *et al.*, page 3, lines 49-52).

The selection of the fatty acid is not of significance to Miettenen *et al.*, because the fatty acid moiety is provided merely for the purpose of making the sterol more soluble in oil. Miettenen *et al.* make no mention of omega-3 fatty acids, particularly EPA, DHA, or SA as presently claimed. Miettenen *et al.* do not recognize the presently claimed advantages of the triglyceride-lowering properties of DHA, EPA and SA, as these are irrelevant to Miettenen *et al.*'s purposes. Moreover, Miettenen *et al.* are silent as to lowering triglyceride levels.

The Leaf *et al.* reference [please note that Leaf is the surname, not Alexander] is a review article that discusses the cardiovascular effects of n-3 (i.e. omega-3) fatty acids, particularly in Eskimos consuming a diet high in fish. The articles teaches that consumption of EPA and DHA, two long chain n-3 fatty acids found in fish oil, but not vegetable oils, lowers serum triglyceride levels. Leaf *et al.* do cite studies concluding that omega-3 fatty acids also may reduce serum cholesterol levels (paragraph bridging pages 549-550), but recognize that the reports in the literature are inconsistent, and that further study is needed (page 550, second column).

This controversy was addressed in Harris (1989) J. Lipid Res. 30:785-807, discussed in the instant application at page 7, lines 25-27, and submitted to the Patent Office previously in this application in an Information Disclosure Statement. Harris concluded that fish oil consumption results either in no change in serum cholesterol, or actually leads to an increase in LDL cholesterol level. There is now consensus that fish oil consumption may indeed lead to increased LDL-cholesterol level, rather than decreased cholesterol levels as presently claimed. In this respect, the art teaches away from the claimed sterol

ester of an omega-3 fatty acid, because the skilled person would conclude that the omega-3 fatty acid would negate the cholesterol-lowering activity of the sterol moiety.

In any event, Leaf *et al.* make no mention whatsoever of sterol esters of omega-3 fatty acids, or their advantages, as presently claimed.

Like Miettenen *et al.*, Mitchell teaches only sterol esters of fatty acids that are not omega-3 fatty acids, contrary to the instant claims. Mitchell does not teach or suggest omega-3 fatty acids, let alone EPA, DHA or SA as instantly claimed, and is silent as to the benefits of using an omega-3 fatty acid.

Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because there is no suggestion or motivation in the references themselves or in knowledge generally available to those of ordinary skill in the art to combine the teachings of Miettenen *et al.* and Leaf *et al.*, or to modify the teaching of Mitchell, as proposed by the Examiner. The references are silent with respect to the desirability of a sterol ester of an omega-3 fatty acid selected from the group consisting of EPA, DHA and SA as instantly claimed. Moreover, in contrast to the surprising results shown in the declaration of Dr. Stephen Ewart, discussed above, none of the references teach or suggest that a sterol ester of an omega-3 fatty acid is useful for reducing levels of both cholesterol and triglycerides.

Applicant respectfully submits that the Examiner is impermissibly using hindsight of the instant application to combine or modify the cited references. The teaching or suggestion to make the claimed combination and the reasonable expectation of success in making the combination must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections of the claims. Should the Examiner be of the view that a telephone conference would expedite prosecution of this application, she is respectfully requested to call the undersigned at the below-listed number.

Respectfully submitted,

BY _____
(Mrs.) Joy D. Morrow
Registration No. 30911

Date: April 15, 2002

Version With Markings t Show Changes Made

Claim 1 has been rewritten as follows:

1. (thrice amended) [A nutritional supplement comprising a sterol eter of an omega-3 fatty acid derived from fish oil, for lowering cholesterol and triglyceride levels in the blood stream of a subject.] A nutritional supplement for lowering cholesterol and triglyceride levels in the blood stream of a subject, said nutritional supplement comprising: a sterol ester of an omega-3 fatty acid, wherein said omega-3 fatty acid is selected from the group consisting of eicosapentaenoic acid 20:5ω3 (EPA), docosahexaenoic acid 22:6ω3 (DHA) and stearidonic acid 18:4ω3 (SA).

Claim 34 has been rewritten as follows:

34. (once amended) The nutritional supplement according to claim 1, [wherein the omega-3 fatty acid is a mixture of fatty acids] comprising a sterol ester of eicosapentaenoic acid 20:5ω3 (EPA) and a sterol ester of docosahexaenoic acid 22:6ω3 (DHA).

Claims 36 and 38 have been cancelled.